US007621907B2

(12) **United States Patent**
Rodstrom

(10) **Patent No.: US 7,621,907 B2**
(45) **Date of Patent: Nov. 24, 2009**

(54) **IMPLANTABLE DRUG DELIVERY SYSTEM**

(75) Inventor: **Theron Robert Rodstrom**, Fort Worth, TX (US)

(73) Assignee: **Alcon, Inc.**, Hunenberg (CH)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 58 days.

(21) Appl. No.: **10/385,791**

(22) Filed: **Mar. 11, 2003**

(65) **Prior Publication Data**

US 2003/0176854 A1 Sep. 18, 2003

Related U.S. Application Data

(60) Provisional application No. 60/363,150, filed on Mar. 11, 2002.

(51) **Int. Cl.**
A61K 9/22 (2006.01)

(52) **U.S. Cl.** **604/892.1**

(58) **Field of Classification Search** 604/890.1, 604/891.1, 892.1, 93.01
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

3,416,530	A	12/1968	Ness	128/260
3,432,592	A	3/1969	Speiser et al.	424/19
3,828,777	A	8/1974	Ness	128/260
3,845,770	A	11/1974	Theeuwes et al.	128/260
3,916,899	A	11/1975	Theeuwes et al.	128/260
3,921,632	A	11/1975	Bardani	128/217
4,008,864	A	2/1977	Torphammar et al.	242/107.4 R
4,034,756	A *	7/1977	Higuchi et al.	604/892.1
4,063,064	A	12/1977	Saunders et al.	219/121 L
4,088,864	A	5/1978	Theeuwes et al.	219/121 LM
4,144,317	A	3/1979	Higuchi et al.	424/21
4,200,098	A	4/1980	Ayer et al.	128/260
4,201,210	A	5/1980	Hughes et al.	128/260
4,220,153	A *	9/1980	Dresback	424/438
4,285,987	A	8/1981	Ayer et al.	427/3
4,300,557	A	11/1981	Refojo et al.	128/260
4,304,765	A	12/1981	Shell et al.	424/14
4,451,254	A	5/1984	Dinius et al.	604/62
4,601,893	A	7/1986	Cardinal	424/15
4,668,506	A	5/1987	Bawa	424/429
4,687,660	A	8/1987	Baker et al.	424/465
4,801,460	A	1/1989	Goertz et al.	424/465

(Continued)

FOREIGN PATENT DOCUMENTS

EP 1 347 741 B1 1/2009

(Continued)

OTHER PUBLICATIONS

http://www.medscape.com—"Biocapsule May Offer New Insulin Delivery System" (Nov. 7, 2001).

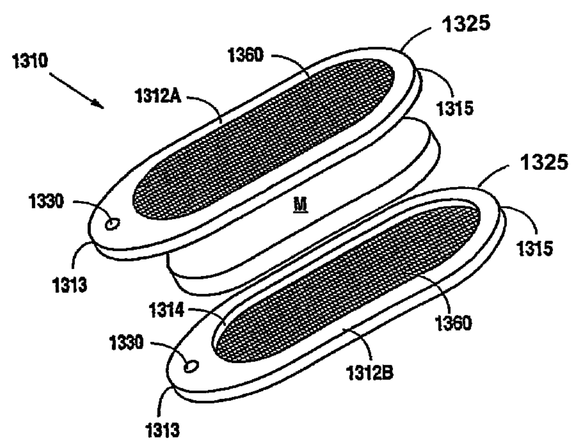
(Continued)

Primary Examiner—Kevin C Sirmons
Assistant Examiner—Elizabeth R Moulton
(74) *Attorney, Agent, or Firm*—Scott A. Chapple

(57) **ABSTRACT**

An implantable medicament delivery device includes a core body which further includes a single basin or multiple smaller basins for containing a drug or a medicament. Each basin is covered by a screen. The implantable drug delivery device is placed within the body of an animal, and the drug is allowed to diffuse through the holes in the screen to provide treatment of a disease or condition.

13 Claims, 14 Drawing Sheets



U.S. PATENT DOCUMENTS

4,806,337	A		2/1989	Snipes et al.	71/65
4,853,224	A		8/1989	Wong	424/427
4,959,217	A		9/1990	Sanders et al.	424/473
4,997,652	A		3/1991	Wong	424/428
5,004,601	A		4/1991	Snipes	424/78
5,004,614	A		4/1991	Staniforth	424/466
5,006,342	A		4/1991	Cleary et al.	424/445
5,082,655	A		1/1992	Snipes et al.	424/386
5,128,145	A	*	7/1992	Edgren et al.	604/892.1
5,164,188	A		11/1992	Wong	424/428
5,314,471	A		5/1994	Brauker et al.	623/11
5,476,511	A		12/1995	Gwon et al.	623/4
5,516,522	A		5/1996	Peyman et al.	424/426
5,582,838	A		12/1996	Roark et al.	424/472
5,660,847	A		8/1997	Magruder et al.	424/424
5,693,335	A		12/1997	Xia et al.	424/448
5,770,076	A		6/1998	Chu et al.	210/490
5,797,898	A		8/1998	Santini, Jr. et al.	604/890
5,798,042	A		8/1998	Chu et al.	210/490
5,824,072	A		10/1998	Wong	623/4
5,824,074	A		10/1998	Koch	623/6
5,836,935	A		11/1998	Ashton et al.	
5,869,079	A		2/1999	Wong et al.	424/426
5,882,682	A		3/1999	Rork et al.	424/473
5,893,974	A		4/1999	Keller et al.	210/483
5,902,598	A	*	5/1999	Chen et al.	604/892.1
5,938,923	A		8/1999	Tu et al.	210/490
5,972,369	A		10/1999	Roorda et al.	424/424
5,985,328	A		11/1999	Chu et al.	424/489
6,044,981	A		4/2000	Chu et al.	210/490
6,107,102	A		8/2000	Ferrari	436/518
6,251,090	B1		6/2001	Avery et al.	604/9
6,331,313	B1		12/2001	Wong et al.	424/427
6,740,077	B1	*	5/2004	Brandau et al.	604/892.1
2002/0086051	A1		7/2002	Viscasillas	424/451
2002/0188282	A1		12/2002	Greenberg	604/890.1
2004/0180075	A1		9/2004	Robinson et al.	

FOREIGN PATENT DOCUMENTS

WO	WO 94/18956	9/1994
WO	WO 97/11655	4/1997
WO	WO 98/00107	1/1998
WO	WO 99/11244	3/1999
WO	WO 00/62760	10/2000
WO	WO 01/80825 A2	1/2001
WO	WO 02/055058 A2	7/2002
WO	WO 03/020172 A1	3/2003

OTHER PUBLICATIONS

Press Release—National Science Foundation PR 01-87, Oct. 30, 2001—"Biocapsule Can Provide Steady Insulin Supply; Potential Breakthrough for Diabetes Patients".

http://192.148.246.31—"Intelligent Micro-Engineered Drug Delivery—Summary" by Carl F. Grove, iMEDD, Inc. (Apr. 2000).

"Technology Opportunity: Micro- and Nanotechnologies for Medical Therapeutics: Stealth Cell Transplantation, Implantable Enzymatic Reactor, Drug Delivery", National Aeronautics and Space Administration.

"Microsystem for Controlled, Continuous Drug Delivery", National Aeronautics and Space Administration (May 2002).

* cited by examiner

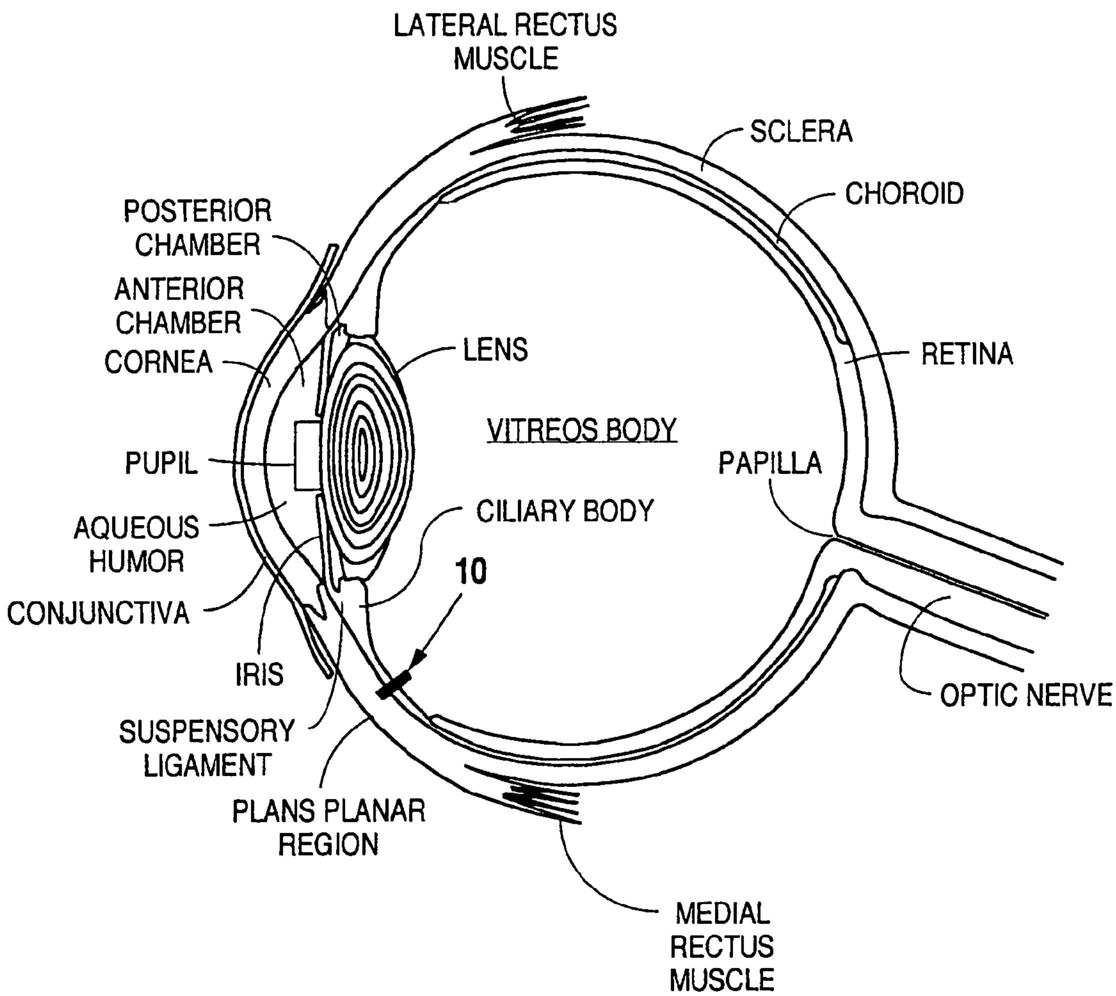

LATERAL RECTUS MUSCLE
SCLERA
CHOROID
POSTERIOR CHAMBER
ANTERIOR CHAMBER
CORNEA
LENS
RETINA
VITREOS BODY
PUPIL
PAPILLA
AQUEOUS HUMOR
CILIARY BODY
10
CONJUNCTIVA
IRIS
OPTIC NERVE
SUSPENSORY LIGAMENT
PLANS PLANAR REGION
MEDIAL RECTUS MUSCLE

Fig. 1

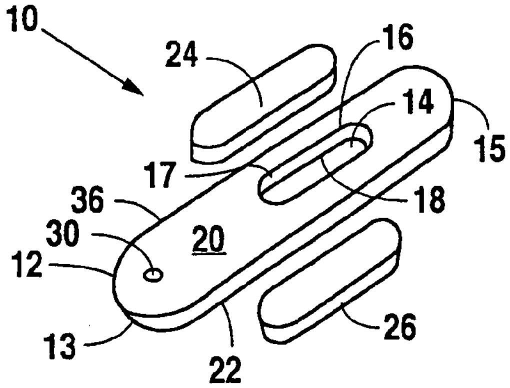


Fig. 2A

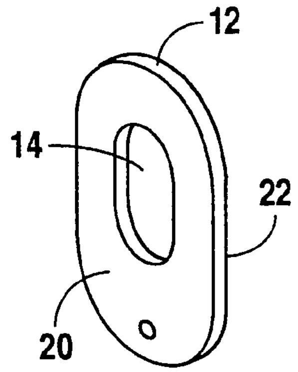


Fig. 2B

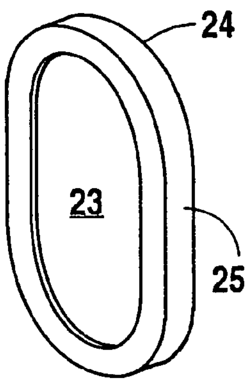


Fig. 2C

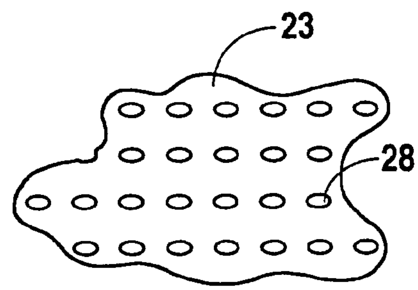


Fig. 2D

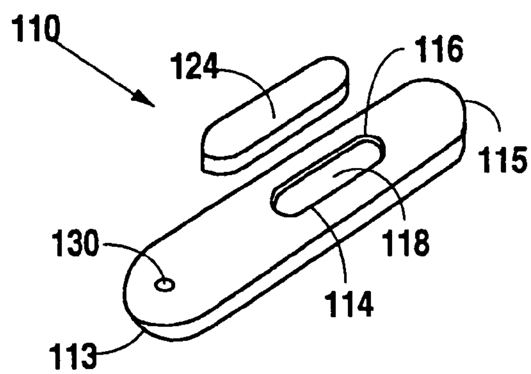


Fig. 3

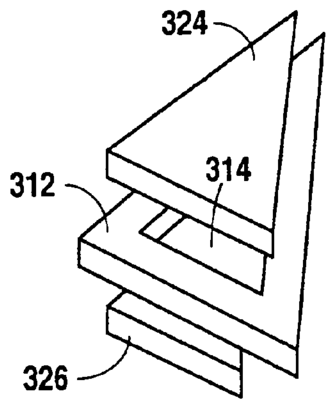


Fig. 4A

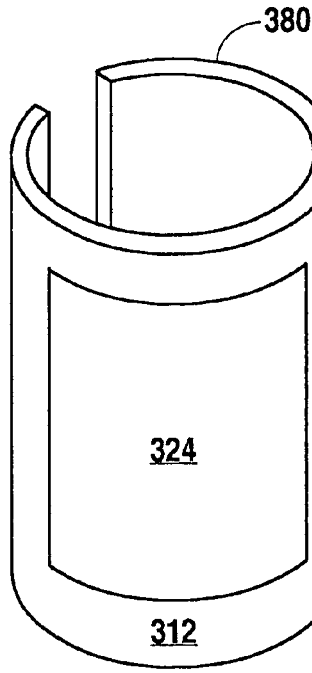


Fig. 4B

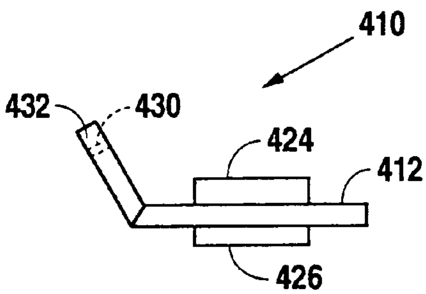


Fig. 5

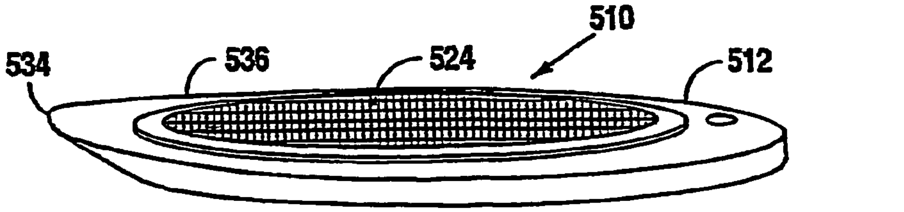


Fig. 6A

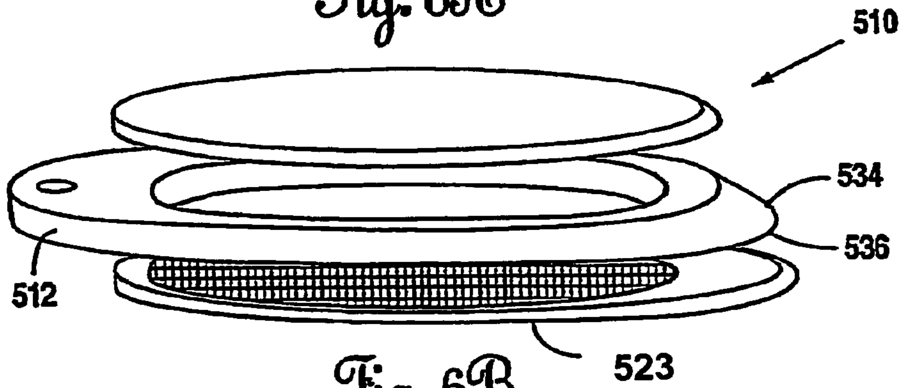


Fig. 6B

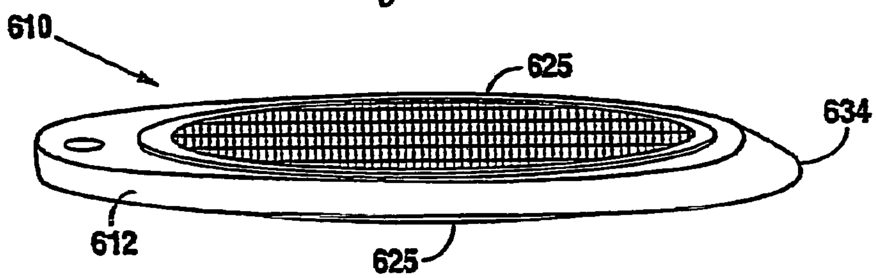


Fig. 6C

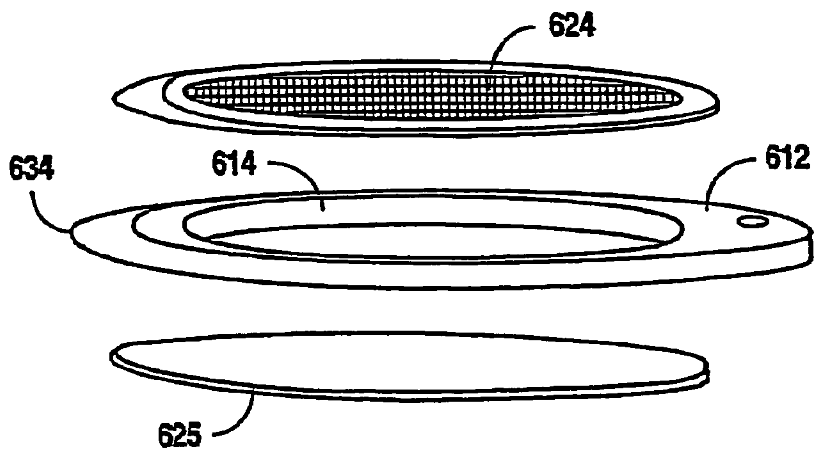


Fig. 6D

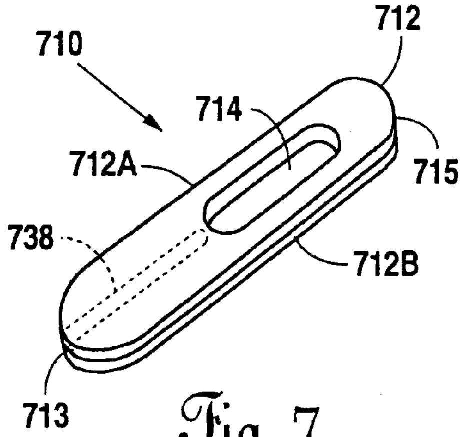


Fig. 7

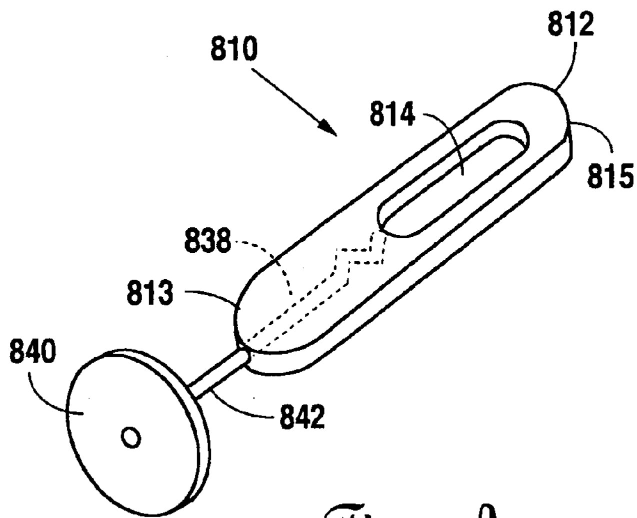


Fig. 7A

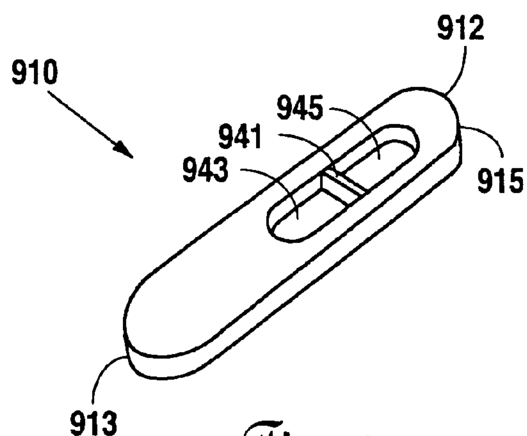


Fig. 8

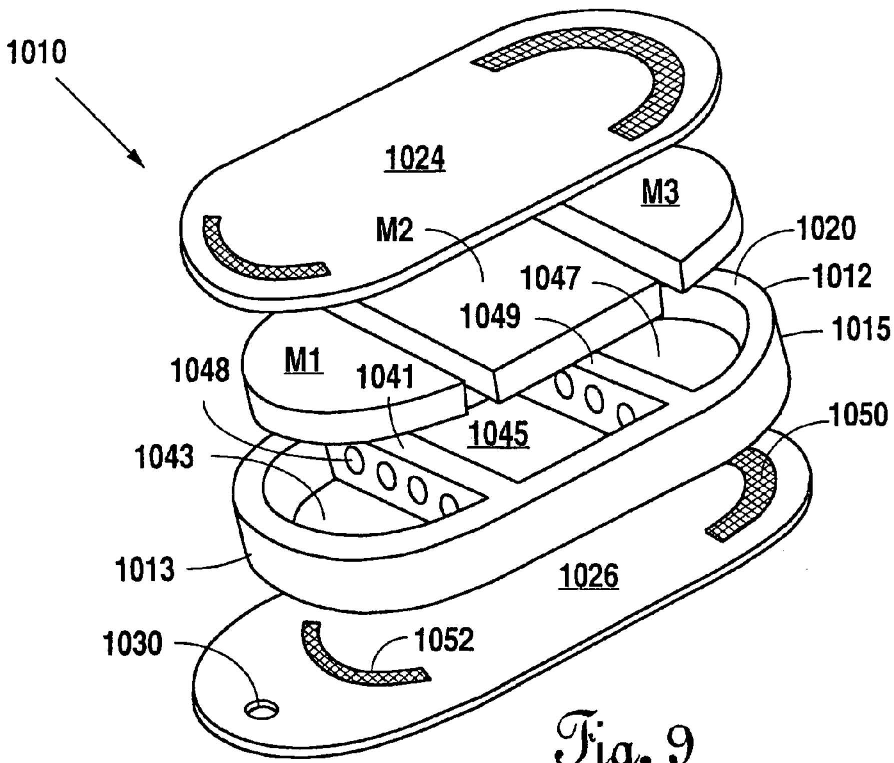

1010
1024
M3
M2
1020
1047
1012
1049
1015
M1
1048
1041
1045
1050
1043
1013
1026
1030
1052

Fig. 9

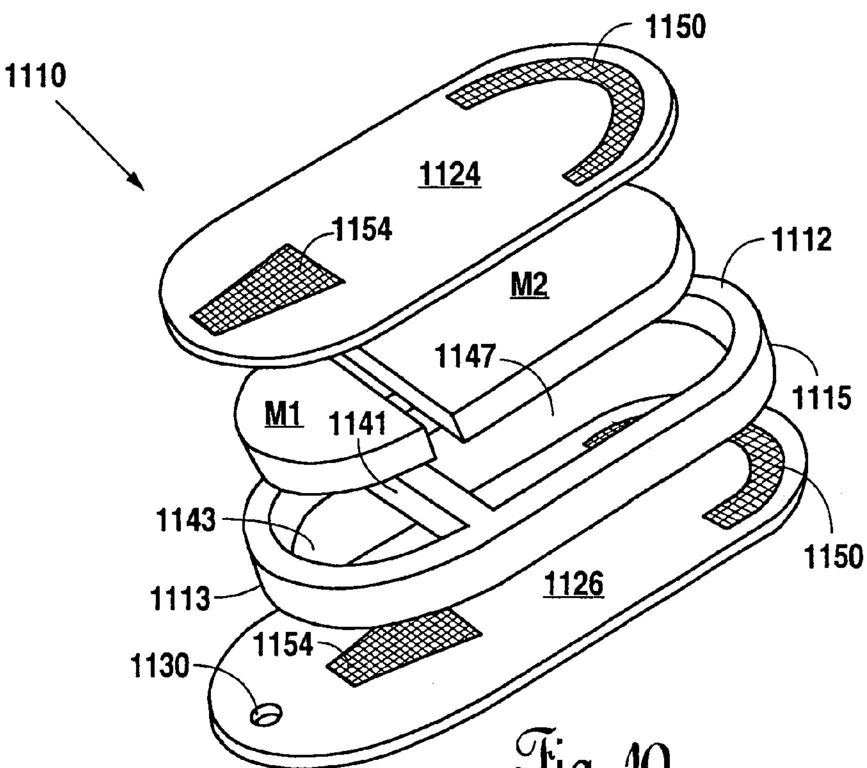

1150
1110
1124
1154
1112
M2
1147
1115
M1
1141
1143
1150
1113
1126
1154
1130

Fig. 10

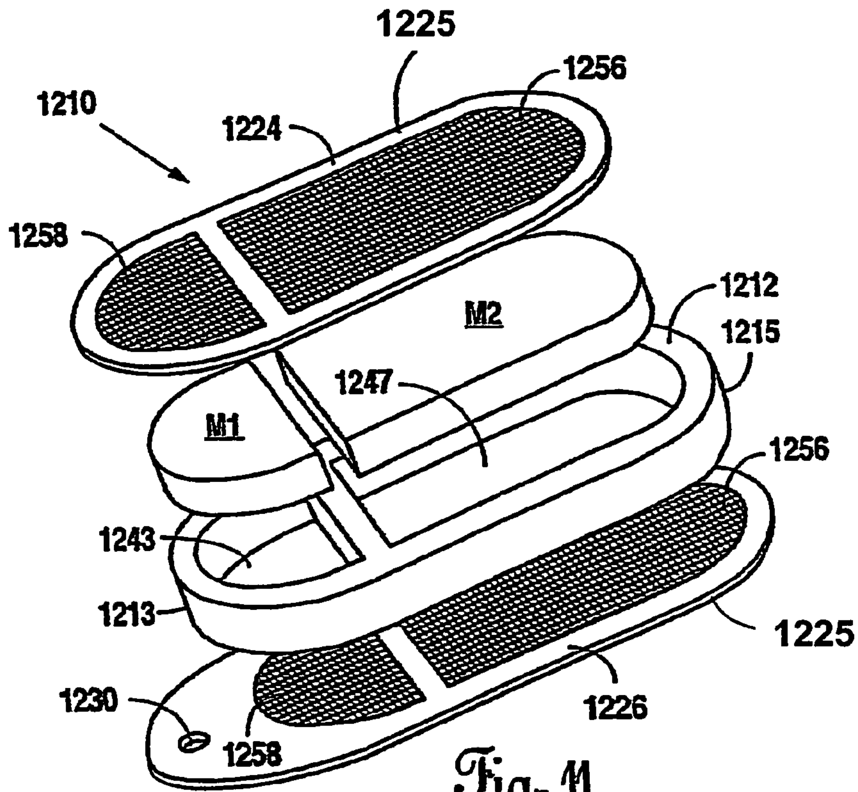

1225
1256
1210
1224
1258
M2
1212
1215
1247
M1
1256
1243
1213
1225
1230
1226
1258

Fig. 11

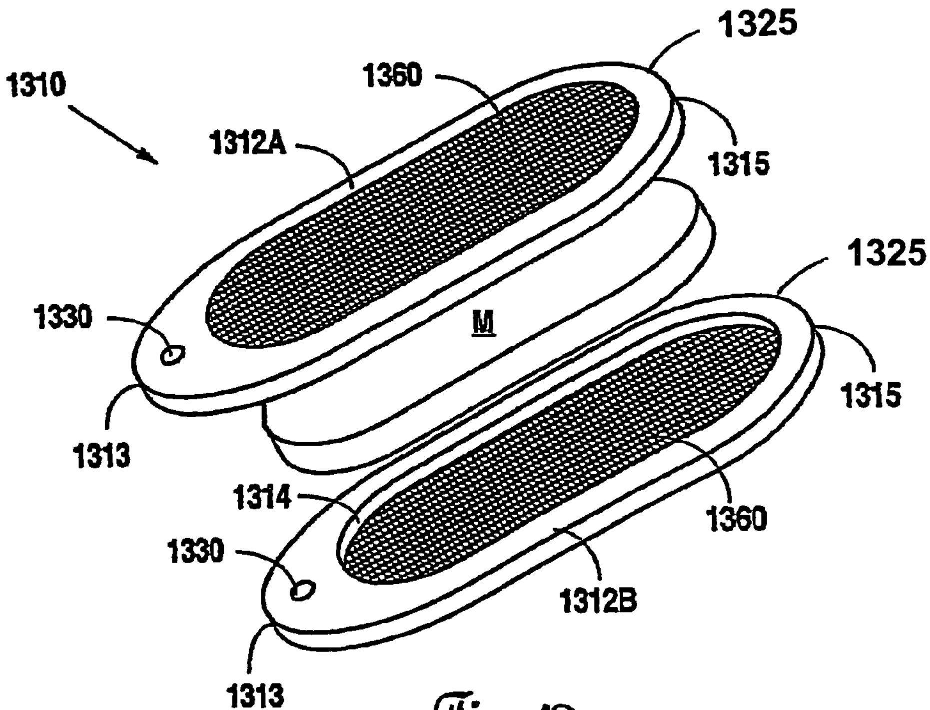

1325
1310
1360
1312A
1315
1325
1330
M
1315
1313
1314
1360
1330
1312B
1313

Fig. 12

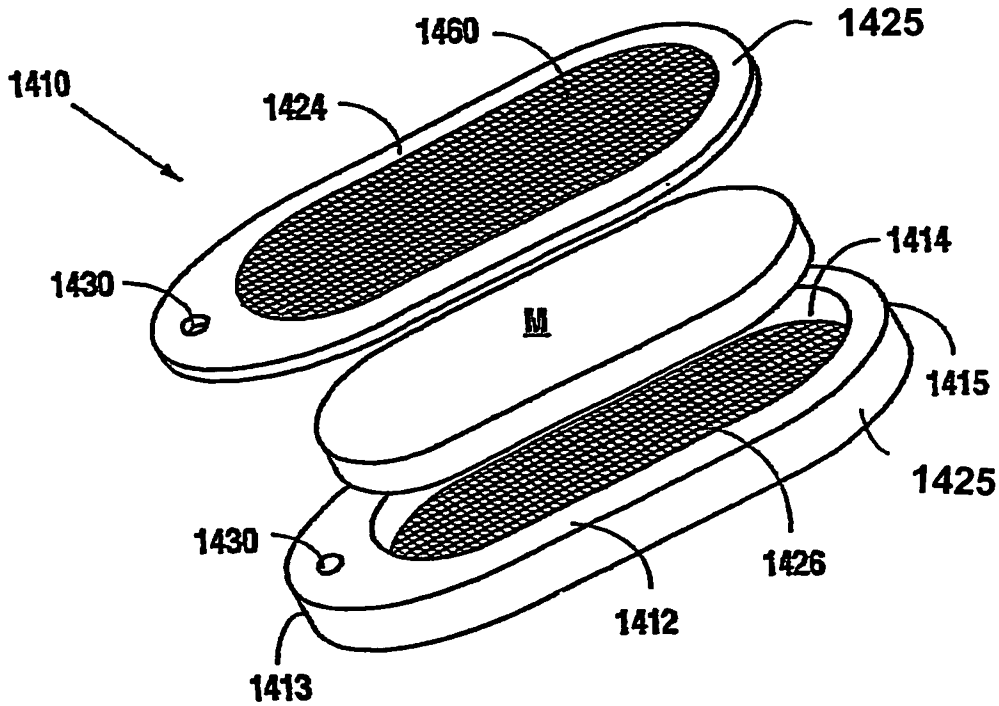

1460
1425
1410
1424
1414
1430
M
1415
1425
1430
1426
1412
1413

Fig. 13

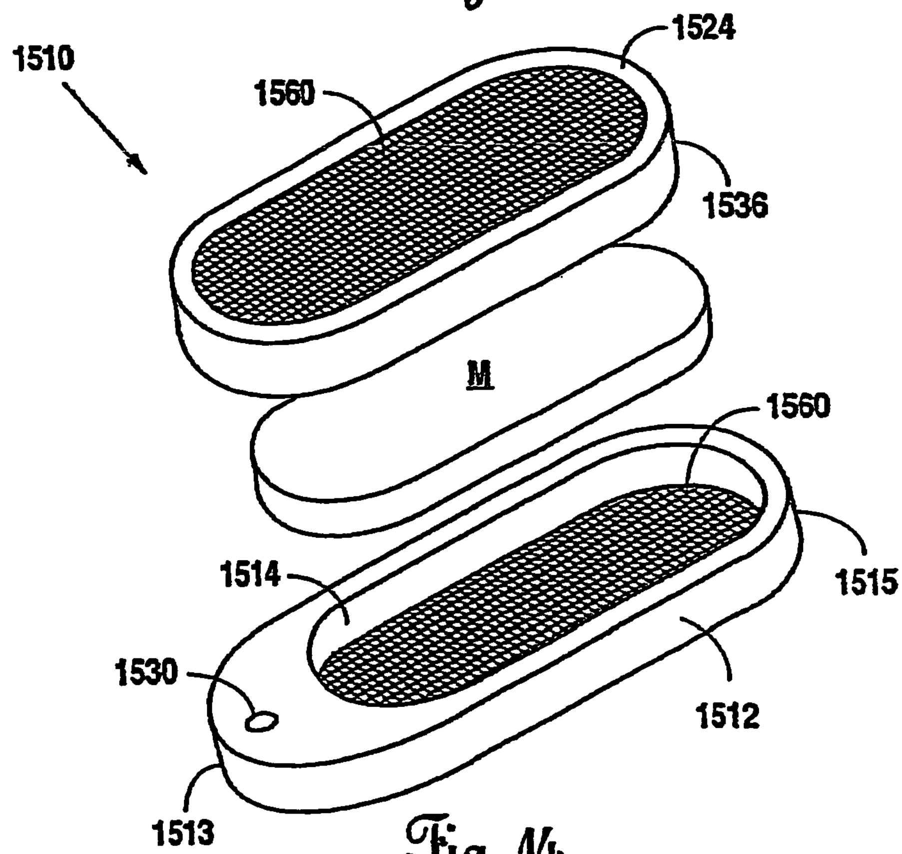

1524
1510
1560
1536
M
1560
1514
1515
1530
1512
1513

Fig. 14

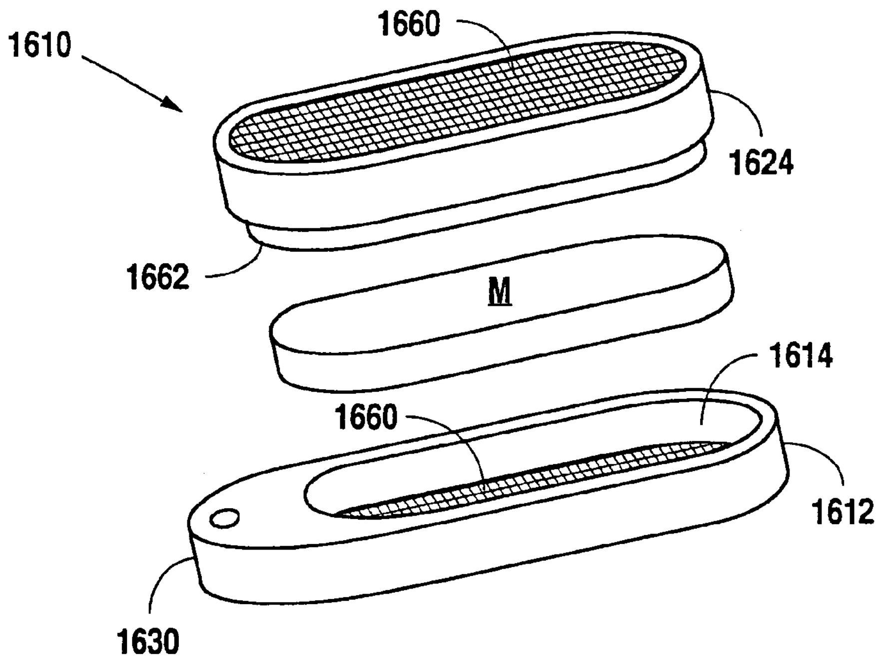

1610
1660
1624
1662
M
1614
1660
1612
1630

Fig. 15

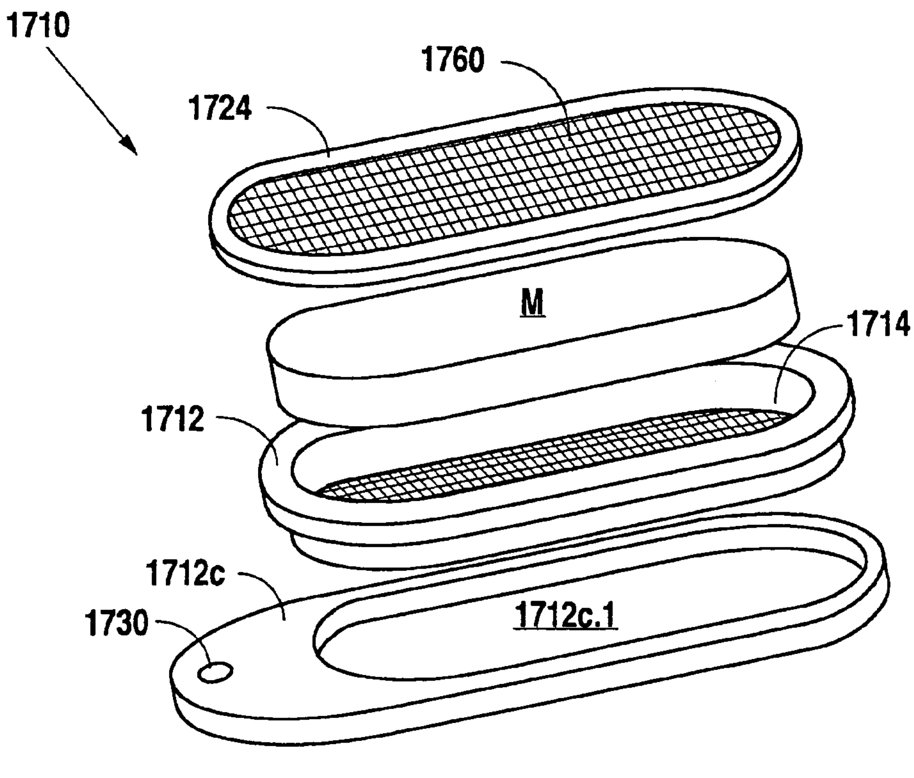

1710
1760
1724
M
1714
1712
1712c
1730
1712c.1

Fig. 16

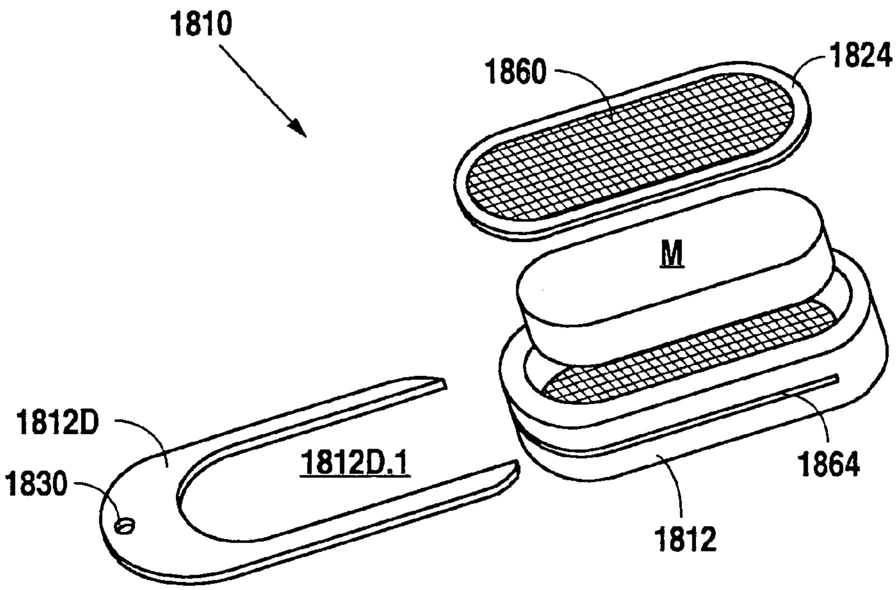

1810
1860
1824
M
1812D
1812D.1
1830
1864
1812

Fig. 17

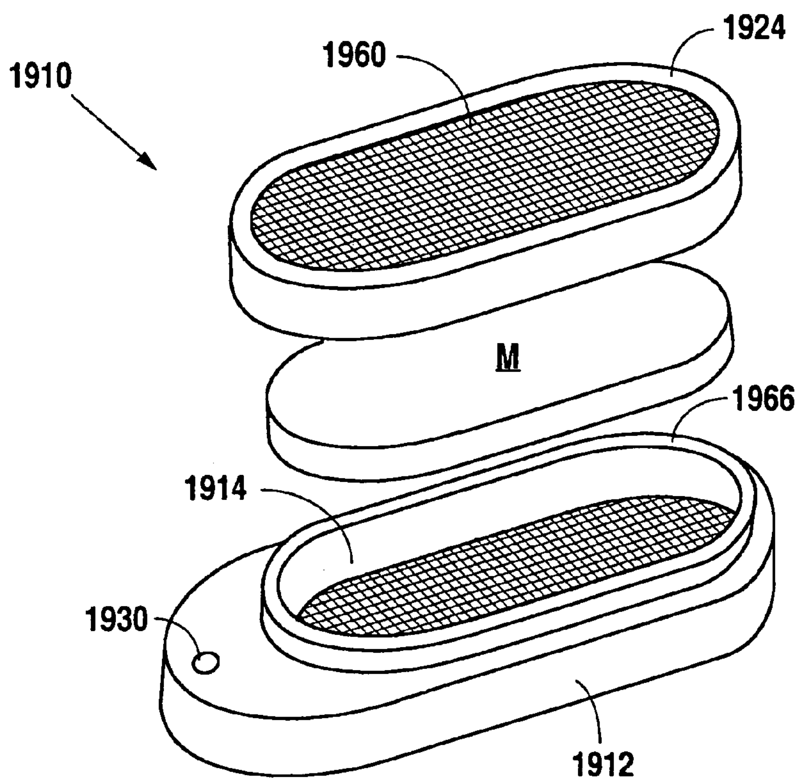

1910
1960
1924
M
1966
1914
1930
1912

Fig. 18

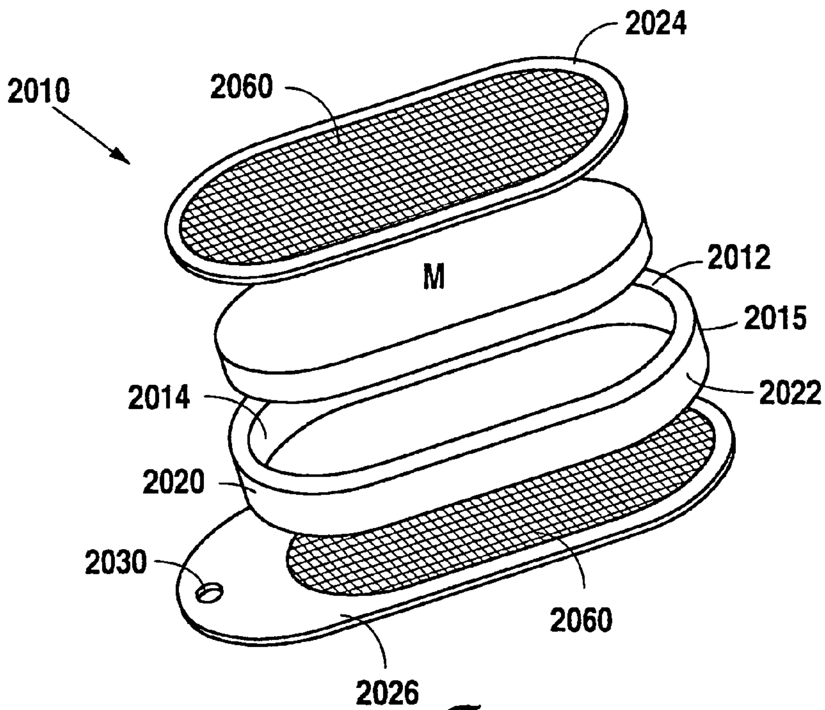

2010
2060
2024
M
2012
2015
2014
2022
2020
2030
2060
2026

Fig. 19

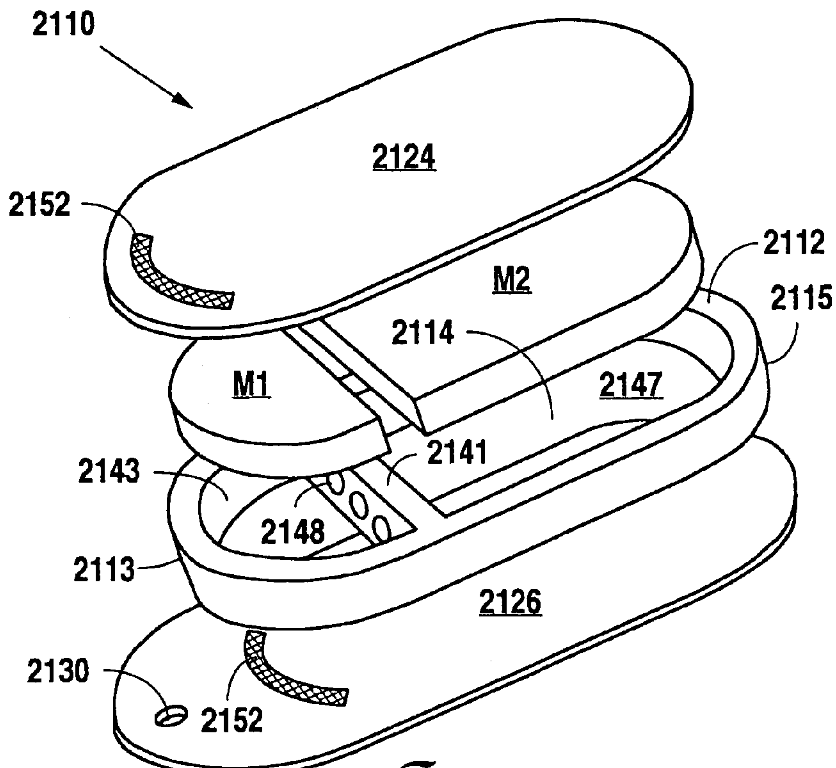

2110
2124
2152
M2
2112
2115
2114
M1
2147
2141
2143
2148
2113
2126
2130
2152

Fig. 20

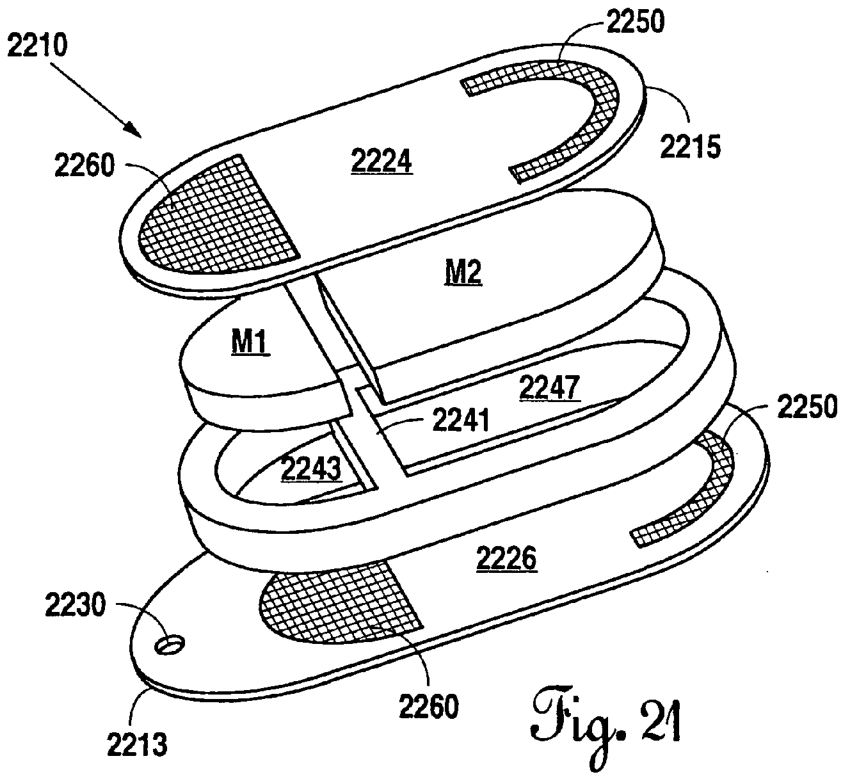

2210
2250
2215
2224
2260
M2
M1
2247
2241
2250
2243
2226
2230
2260
2213

Fig. 21

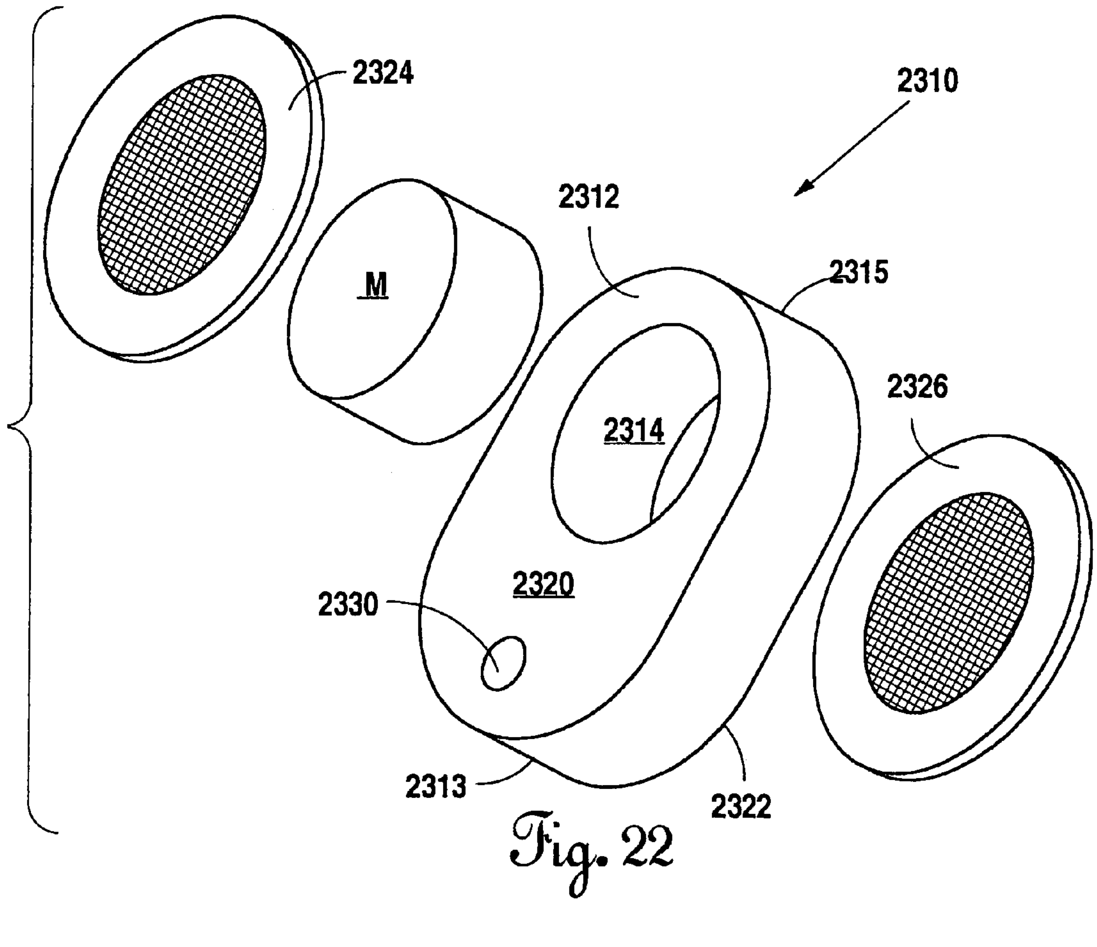

2324
2310
M
2312
2315
2326
2314
2320
2330
2313
2322

Fig. 22

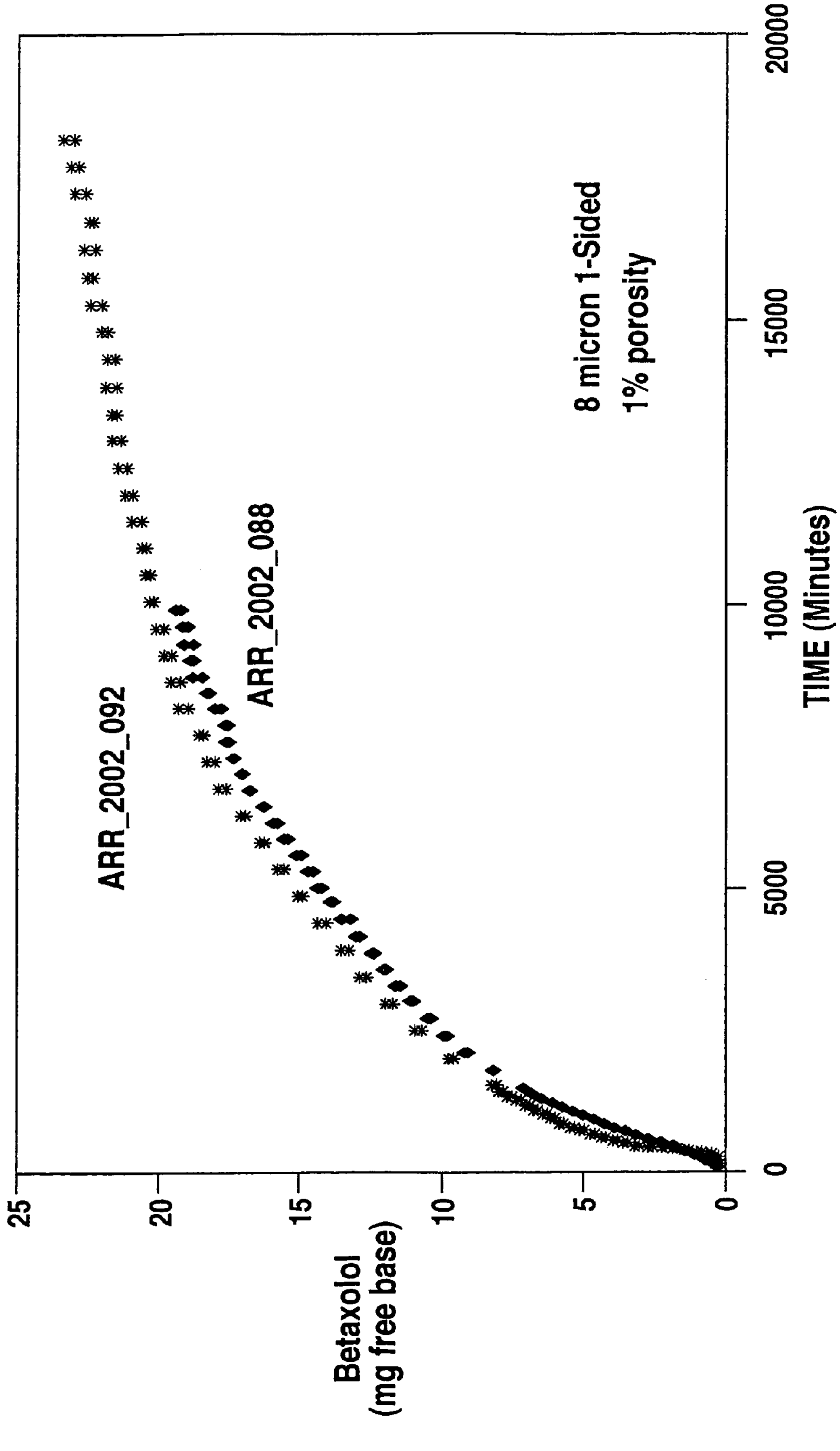

Betaxolol (mg free base)
25
20
15
10
5
0
0
5000
10000
15000
20000
TIME (Minutes)
ARR_2002_092
ARR_2002_088
8 micron 1-Sided
1% porosity

Fig. 23

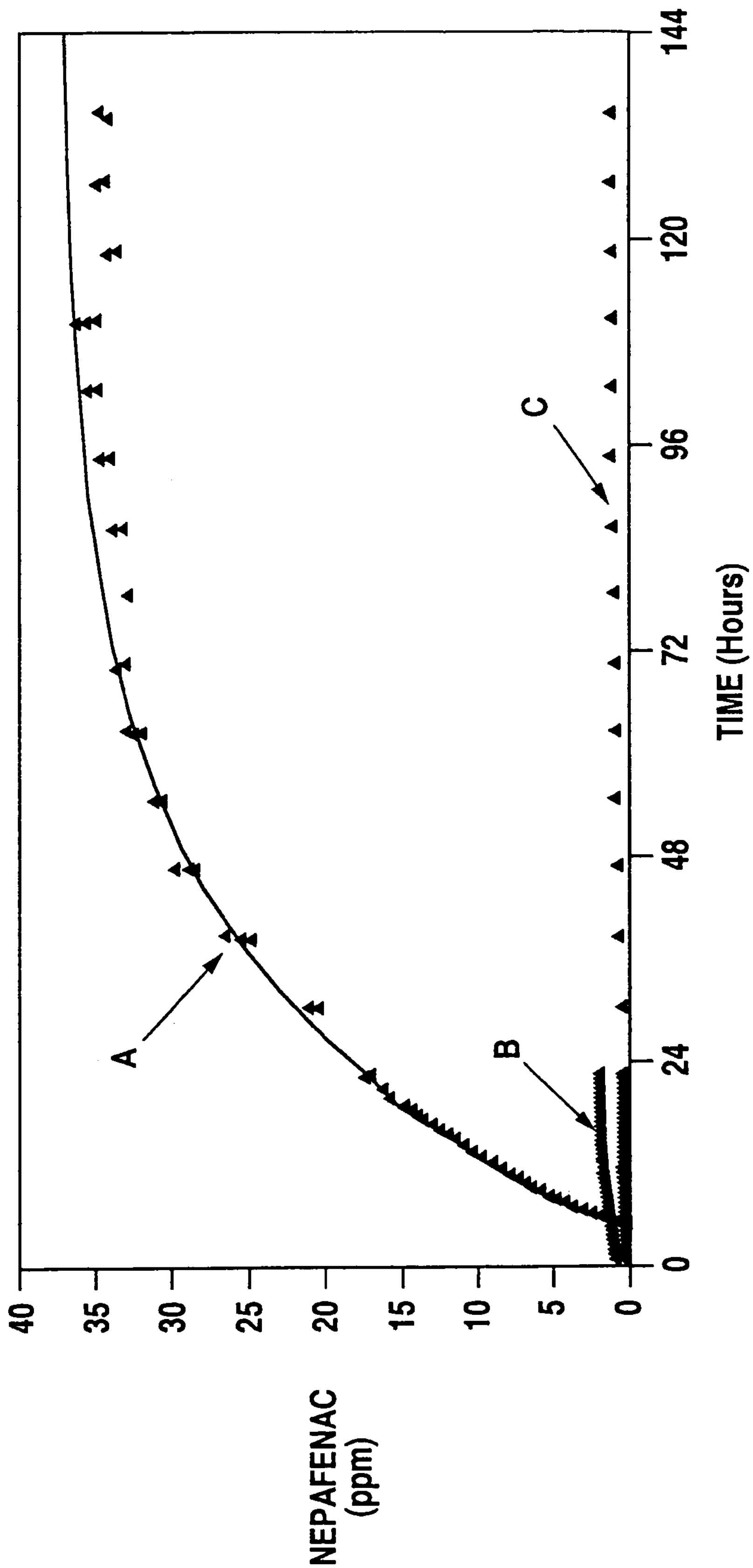

NEPAFENAC
(ppm)
0
5
10
15
20
25
30
35
40
TIME (Hours)
0
24
48
72
96
120
144
A
B
C

Fig. 24

IMPLANTABLE DRUG DELIVERY SYSTEM

This application claims priority from U.S. Provisional Patent Application Ser. No. 60/363,150 filed Mar. 11, 2002.

FIELD

The present invention pertains to a drug delivery system; more particularly, the present invention pertains to an implantable small drug delivery device for use with human beings or other animals.

BACKGROUND

There are many conditions or diseases which occur within the body of a human being or an animal which respond effectively to treatment by the use of one or more medicaments. For many such conditions and diseases the medicament is taken orally. Once swallowed, the medicament eventually migrates to the location of the condition or disease by passing through the gastrointestinal system. In still other instances, medicament is delivered to the location of the condition or disease through the bloodstream. Specifically, the medicament is injected by a syringe into a muscle or soft tissue and then carried by the flow of blood. In still other situations, generally in a health care facility, an IV drip may be used to place the medicament directly into a blood vessel. In yet other situations, some type of surgical intervention is used to physically place a particular medicament within the body at or near the location of a condition or disease.

It has been found that by use of the techniques developed for the creation of integrated circuits, small drug delivery devices can be manufactured which may be used to both contain and then deliver medicament to the site of a condition or disease within the human body. Examples of such small drug implantation devices are disclosed in the following U.S. patents: U.S. Pat. No. 5,770,076; U.S. Pat. No. 5,797,898; U.S. Pat. No. 5,985,328; U.S. Pat. No. 6,123,861, and U.S. Pat. No. 6,331,313. Many of these small drug implantation devices are highly complex and, accordingly, both difficult and expensive to manufacture. Thus, there remains a need in the art for a simple, low cost, easy-to-manufacture implantable small drug delivery device that can be adapted for implantation within the body of a human being or other animal to deliver medicament to a wide variety of locations.

SUMMARY

The simple, low cost, easy-to-manufacture implantable drug delivery system of the present invention enables the implantation of a mechanism within the body to deliver medicament to a wide variety of locations. The disclosed system includes at least one basin, well, or open space. The basin, well, or open space is enframed, enclosed, encased, or formed in a core body. The basin, well, or open space within the core body or basin encasement portion is of sufficient size to contain the desired amount of a medicament needed for prolonged internal treatment of a chronic condition or disease. Typical of such chronic conditions or diseases are those that are known to occur within the eye.

Covering the basin, well, or open space which is surrounded by the core body, at either the top, the bottom, or both, is a banded screen encircled by a band. The banded screen is used to control the release or movement of a drug or a medicament from a tablet, a powder, or a slurry placed in the basin, well, or open space into the body of a human or an animal. The number, size, location, and arrangement of the empty or clear holes in the banded screen or banded screens is a function of the solubility of the medicament contained in the basin, well, or open space, the dissolution rate of the medicament, the concentration of the medicament, and the form of the medicament—be it a tablet, a powder, a slurry, or a combination thereof.

Once one or more medicaments have been placed into the basin, well, or opening, and the basin, well, or opening is covered with the screen encircled by a band, the entire combination of the drug or medicament, the core body in which the basin is formed, and the banded screen is implanted within the body. For example, for conditions or diseases occurring within the eye, one technique is to insert the disclosed drug delivery system into the eye through the sclera portion. Once the disclosed drug device have been properly positioned at its desired location, it may be affixed in place using a variety of methods, to include passing sutures through a hole formed in the core body.

Dispersion of the medicament out of the basin, well, or open space occurs when fluid from the body moves through the empty or clear holes in the banded screen into the basin. This flow of fluid through the empty or clear holes in the banded screen initiates the dissolution of the medicament within the basin. The dissolved medicament will then slowly diffuse outwardly through the empty or clear holes in the banded screen to provide continuing treatment of the condition or disease as long as a quantity of medicament remains within the basin of the disclosed drug delivery device. More particularly, there is a bi-directional free flow through the holes in the banded screen both into and out of the basin. The only flow volume limiting factor is the size of the holes in the banded screen.

DESCRIPTION OF THE DRAWING FIGURES

A better understanding of the implantable drug delivery system of the present invention may be had by reference to the drawing figures, wherein:

FIG. **1** is a side elevational view of an embodiment of the invention inserted into a human eye;

FIG. **1**A is an exploded perspective view of the preferred embodiment;

FIG. **2**B is a perspective view of a core body similar to that shown in FIG. **2**A;

FIG. **2**C is a perspective view of a banded screen encircled by a band similar to that shown in FIG. **2**A;

FIG. **2**D is a magnified planar view of a portion of a screen encircled by a band such as shown in FIG. **2**C.

FIG. **3** is an exploded perspective view of a first alternate embodiment;

FIGS. **4**A and **4**B are perspective view of a first alternate embodiment;

FIG. **5** is a side elevational view of the drug delivery system attached to a support piece;

FIG. **6**A is a perspective view of the drug delivery system including a sharpened edge or scalpel nose portion;

FIG. **6**B is an exploded view of the embodiment shown in FIG. **6**A;

FIG. **6**C is a perspective view of the drug delivery system including a sharpened edge similar to that shown in FIG. **6**A;

FIG. **6**D is an exploded view of the embodiment shown in FIG. **6**C;

FIG. **7** is a perspective view of an alternate embodiment of the core body of the drug delivery system of the present invention further including a channel for the resupply of medicament to the basin;

FIG. **7**A is an alternate embodiment of the core body of the drug delivery system shown in FIG. **7**, including a flanged portion; and

FIG. **8** is a perspective view of yet another alternate embodiment of the drug delivery system, including multiple smaller basins;

FIG. **9** is a perspective view of a drug delivery system having a three compartment basin including internal passageways for medicament migration between compartments;

FIG. **10** is a perspective view of a drug delivery system including two smaller basin within a larger basin

FIG. **11** is a perspective view of an alternate embodiment of the drug delivery system shown in FIG. **10**;

FIG. **12** is a perspective view of a drug delivery system having a single basin;

FIG. **13** is a perspective view of a first alternate embodiment of the drug delivery system shown in FIG. **12**;

FIG. **14** is a perspective view of a second alternate embodiment of the drug delivery system shown in FIG. **12**;

FIG. **15** is a perspective view of a third alternate embodiment of the drug delivery system shown in FIG. **12**;

FIG. **16** is a perspective view of a fourth alternate embodiment of the drug delivery system shown in FIG. **12**;

FIG. **17** is a perspective view of a fifth alternate embodiment of the drug delivery system shown in FIG. **12**;

FIG. **18** is a perspective view of a sixth alternate embodiment of the drug delivery system shown in FIG. **12**;

FIG. **19** is a perspective view of a seventh alternate embodiment of the drug delivery system shown in FIG. **12**;

FIG. **20** is a perspective view of an eighth alternate embodiment of the drug delivery system shown in FIG. **12**;

FIG. **21** is a perspective view of an first alternate embodiment of the drug delivery system shown in FIG. **10**;

FIG. **22** is a perspective view of a second alternate embodiment of the drug delivery system shown in FIG. **10**;

FIG. **23** is a graph of drug concentration over time in an in vitro study using betaxolol HCl tablets; and;

FIG. **24** is graph of drug concentration over time in an in vitro study using nepafenac tablets;

In the following description of the preferred and alternate embodiments, reference numbers are used to facilitate the description of the disclosed invention. Throughout this description, the same numbers in the units and tens places refer to the same portion of each embodiment. The numbers in the hundreds and thousands places are used to designate an alternate embodiment.

As may be seen in FIG. **1**, the present invention is a small implantable drug delivery system **10** shown being used for the treatment of a condition or disease affecting an inner portion of the eye. Such diseases include but are not limited to ARNID (age related macular degeneration), PDR (proliferative diabetic retinopathy), neovascular glaucoma, ischemic and iatrogenic retinopathy, posterior ocular inflammation and retinal edema.

While the preferred embodiment of the present invention is described herein according to its use for treatment of inner eye diseases, it will be understood by those of ordinary skill in the art that the present invention may be used at any location in the body of an animal suitable for the treatment of a disease or condition with medicament contained in a small drug delivery device.

In addition to treatment of the diseases of the eye, the drug delivery device according to the present invention could be positioned adjacent to the prostate gland in men for the treatment of prostate cancer or benign prostate hyperplasia. By using the disclosed device, the negative side effects normally associated with the treatment of prostate cancer, such as hot flashes, vocal changes, or breast enlargement could be significantly reduced or even eliminated. In addition, those of ordinary skill in the art will understand that the amount of a drug or medicament needed for treatment of a disease or condition could be significantly reduced, thus reducing patient cost. Patient compliance with a treatment regimen would improve as the need for frequent drug administration would effectively be eliminated. Pharmacist workload and exposure to hazardous or toxic pharmaceuticals would be reduced. The opportunity for drug-drug or drug-food interaction would be effectively avoided. And, the opportunity to provide drug combination therapy would be increased.

Similar advantages could also be obtained if the disclosed device instead included a contraceptive implanted within a female. Still other potential applications include the treatment of vaginal fungal infections with an anti-fungal medicament.

Victims of Parkinson's disease would also be candidates for implantation of the disclosed drug delivery device within the brain to slowly release medicament for reduction of tremors. Patients with ulcerative colitis or a variety of different gastroenterological diseases may also be able to obtain relief by implantation of the disclosed device in their GI tract.

As may be seen in FIG. **2**A, the drug delivery system **10** includes a basin **14**. The basin is formed in a basin containment, enframement, or encasement portion **12**. For simplification of description, the basin containment, enframement, or encasement portion is called the core body **12**. In the preferred embodiment, the core body **12** is formed from a substantially planar rigid piece of material. The basin **14** in FIG. **2**A is shown with a top **16** and a bottom **18**. The top **16** of the basin **14** intersects the upper face **20** of the core body **12**. In the preferred embodiment, the bottom **18** of the basin **14** intersects the lower face **22** of the core body **12**. The illustrated basin **14** is effectively a hole which passes through the core body **12**. If the top **16** is larger than the bottom **18**, the basin **14** may have tapered walls **17**.

A still better understanding of the construction of the core body **12** may be had by reference to FIG. **2**B. Therein, the core body **12** is shown having an arcuate modified racetrack outer perimeter. The basin **14** contained therein passes completely therethrough from the upper face **20** to the lower face **22** and has a perimeter roughly parallel to the outer perimeter of the core body. For a better appreciation of the small size of the disclosed drug delivery system, the length of the core body **12** is about 9.5 mm and the width is about 5.3 mm.

The basin **14** may be located at the center of the core body **12** as shown in FIG. **2**B or closer to one end of the core body **12**. The size of the basin **14** is sufficient to hold a variety of different medicaments. Such medicaments may include those that are directly or indirectly a neuro-protectant, an anti-oxidant, an anti-apoptotic agent, a soluble growth factor agonist or antagonist, an anti-proliferative agent, an anti-angiogenic agent, an anti-edematous agent, a vascular targeting agent, an anti-inflammatory, or an antibiotic, whether they be small organic molecules or biologics, such as proteins, ribozymes, antibodies, antibody fragments, aptameters, or oligonucleotides. More specifically, suitable medicaments include, but are not limited to, signal transduction inhibitors, protein kinase antagonists, tyrosine kinase antagonists, VEGF receptor antagonists, integrin antagonists, matrix metalloproteinase inhibitors, glucocorticoids, NSAIDS, COX-1 and/or -2 inhibitors, and angiostatic steroids. Each of these medicaments may be in the form of either a powder, a slurry, or a tablet. The amount of such medicament should be sufficient to provide enough treatment of the disease for which the medicament is prescribed for a predetermined time period, depending on the type and severity of the disease. If desired, a variety of different additives may be added to the medicament to increase its effectiveness. For example, an additive with water affinity, such as an excipient humectant, may be added to the medicament for the purpose of attracting water molecules to the area where the device is inserted into the eye to initiate or to aid dissolution of the medicament or transport of the medicament out of the basin **14**.

To minimize the formation of small bubbles within the basin **14**, it is preferable that the size and shape of the basin **14** and the size and shape of the medicament placed in the basin **14** should be substantially the same to minimize the amount of free air.

As shown in FIG. **2**C, a first screen **24** encircled by a band **25** is formed to be attached to the upper face **20** of the core body **12** to cover the top **16** of the basin **14**. In the preferred embodiment, the banded screen **24** is as shown in FIG. **2**C. Specifically, the banded screen **24** has an arcuate modified race track perimeter **36** which is roughly parallel to the perimeter of the basin **14** and the perimeter of the core body **12**. That portion **23** of the banded screen **24** in which the holes **28** are formed may be of equal thickness with the perimeter or band portion **25** or a different thickness depending on the construction of the device **10**.

As may be seen in FIG. **2**D, the banded screen **24** or banded screens **24**, **26** are formed to include a predetermined pattern of substantially uniform sized holes **28**. The number, size, location, and arrangement of the predetermined pattern of holes **28** in the banded screen **24** or banded screens **24**, **26** is a function of a variety of factors to include the solubility of the drug which is placed in the basin **14**, the dissolution rate of the drug which is placed in the basin **14**, and the concentration of the drug which is placed in the basin **14**. Typically, the size of each individual hole in the predetermined pattern of holes **28** is controlled by the manufacturing process, such as etching, to be anywhere from substantially about 0.2 microns to substantially about 100 microns. However, because of the versatility of the disclosed invention in other applications, a still different range of substantially uniform hole sizes may be used. While it is understood that a generally uniform distribution in the predetermined pattern of the holes **28** over the surface of the banded screen **24** or banded screens **24**, **26** enables maximum dissolution of the medicament, other non-uniform distributions in the predetermined pattern of holes **28** are also possible as explained below. Additionally, those of ordinary skill in the art will understand that when the drug delivery system of the present invention is used within the eye, all holes must be small enough to block the passage of any undissolved particles of medicament which might interfere with vision.

A suitable thickness for each banded screen will be from about 0.05 mm to 0.5 mm: Once the banded screen **24** is formed, the predetermined pattern of holes **28** is formed therein. A suitable thickness of the core body **12** will be from about 0.5 mm to about 3.0 mm, preferably about 1.0 mm to about 2.0 mm, depending on the amount of medicament that is intended to be administered at the target implantation site.

When either metallic or non-metallic materials are used to fabricate the disclosed drug delivery device, the banded screen **24** or banded screens **24**, **26** may be affixed to the core body **12** by attaching the band portion **25** of the banded screen to the core body **12** using a variety of different adhesives, to include silicon rubber, cyano acrylates, or commonly available bio-compatible room temperature adhesives, thermal adhesives, epoxies, or ultraviolet light cured adhesives. In the preferred embodiment, the banded screen **24** or banded screens **24**, **26**, like the core body **12**, are also formed to be substantially planar.

A variety of different materials may be used to fabricate the core body **12** and the banded screens **24**, **26**. Such materials may be selected from a variety of different bio-compatible materials to include silicon, glass, ruby, sapphire, diamond, or ceramic through which holes may be formed. If desired, a bio-compatible metal may be used to form the core body **12** and the banded screens **24**, **26**. Such bio-compatible metals include gold, silver, platinum, stainless steel, tungsten, and titanium through which holes may be formed. When a bio-compatible metal is used the band portion **25** of the banded screen **24** or banded screens **24**, **26** may be welded to the core body **12** using a variety of different techniques, to include laser welding, thermo-electro bonding, as previously indicated, or the glues and adhesives described above.

Those of ordinary skill in the art will understand that the effectiveness of the disclosed drug delivery platform is determined by the delivery of the appropriate number of molecules of medicament through the predetermined pattern of holes **28** during a predetermined period of time. Accordingly, the sum total of the area of the holes **28** in the screen or screens inside the band **25** must enable the desired delivery rate of medicament from the basin **14**. Generally, this is referred to as hole density. For the purposes of this disclosure, hole density is the total area of the holes divided by the total surface area of the device, even that area not covered by the holes within a banded screen.

The number of holes, their size, their location, and their general appearance on the surface of a banded screen forms the predetermined pattern of holes **28**. This predetermined pattern of holes **28** will be adjusted by the physician using the disclosed invention to assure that required amount of medicament is delivered at the needed flow rate. When multiple basins are formed in the core body, multiple hole patterns in the banded screens may be used to control the flow of medicament. For example, a predetermined pattern of holes **28** having holes concentrated at one end of a basin will initially cause a fast flow of medicament. But, as the medicament is used up, the medicament will have a longer path to travel before exiting the basin **14**; accordingly, the release rate of medicament out of the drug delivery basin **14** will drop off over time.

In an alternate embodiment **110** shown in FIG. **3**, the bottom **118** of the basin **114** may itself be formed as a banded screen, thus obviating the need for the use and attachment of a second banded screen **26** as shown in FIG. **2**A. In other applications, as shown in FIG. **3**, it is also possible for the basin **114** to have a solid bottom. When the basin **114** has a solid bottom, only a single banded screen **124** is used on the top **116** of the basin **114**.

While the preferred embodiment shows a modified racetrack perimeter **36** with the basin **14** closer to the distal end **15** and a suture hole **30** placed at the proximal end **13**, it will be understood by those of ordinary skill in the art that numerous other designs of the implantable drug delivery platform are possible without departing from the scope of the present invention. For example, the drug delivery platform may be formed with multiple suture holes **30** or with straight sides such as the triangle shape **310** as shown in FIG. **4**A. Alternatively, a square shape, a circular shape, a paddle shape, or any other convenient shape which may be inserted through a small incision in the eye or located in a portion of the body where the medicament is determined to be most effective may be used.

Because of the adaptability of the disclosed invention to being configured in a variety of different shapes, particularly if the core body and banded screen(s) are formed of a biocompatible metal, the disclosed device may be formed as a ring or in a cylinder **380** having a basin therein, as shown in FIG. **4**B. When configured in this manner, the device may be crimped around a tendon, a ligament, a muscle fiber, a blood vessel, a nerve bundle, or any other part of the body which would respond to local administration of a medicament. Similarly, such cylinder **380** could also be placed within a tubular conduit such as an artery or a vein within the body and either expanded or sutured to affix its position.

If desired, different types of medicaments may be placed in different core bodies having different shapes or different colors. The use of different medicaments in different shaped or colored core bodies will reduce confusion of medications by enabling surgeons to distinguish between medicaments by the shape or color of the device in which the medicament is contained.

In certain situations it may be necessary to orient the drug delivery device in a particular position with regard to the condition or disease being treated. In such situation, the drug delivery device **410** may be attached to a support piece **432** as shown in FIG. **5** to enable a desired orientation of the core body **412**.

In still another embodiment of the drug delivery platform **510** as shown in FIGS. **6**A and **6**B, the core body **512**, the upper banded screen **524**, and a lower plate **523** may be fabricated to form a sharpened edge **534**. While a thin planar embodiment as shown in FIGS. **2**A, **3** and **4**A may be suitable for insertion into the vitreous body of the eye, other applications may require penetration of soft tissue. When the core body **512** is formed such that a portion of the perimeter edge **536** of the core body **512** is formed to include a sharpened edge **534**, the core body **512** itself may be used to make an initial incision or enlarge an incision through which the drug delivery device **510** is placed. In this embodiment, the leading edge of the upper banded screen **524** is that portion of the sharpened edge which is used to make initial contact for creating an opening through which the disclosed drug delivery device may be inserted.

In yet another alternate embodiment **610**, as shown in FIGS. **6**C and **6**D, the sharpened edge may be placed on the portion on the edge of a solid piece **625** located under the basin **614**.

While sufficient medicament can be placed within the basin of the core body to treat the condition or disease for a minimal or prolonged period of time, it may be necessary to actually replace the medicament if the condition or disease is particularly persistent. While the entire device may be replaced, it has been found that when the device is used inside a patient for a prolonged period of time, such as a year or more, the basin **714** within the core body **712** may be refilled by the use of a passageway **738** running from the perimeter edge **736** of the core body **712** into the basin **714** as shown in FIG. **7**. Because of the small size of the core body **712**, it may not be possible to drill a passageway from the perimeter edge **736** to the basin **714**. In such cases, it may be necessary to form the core body **712** from two mating pieces **712**A, **712**B, each mating piece including a partial channel. These two partial channels come together either horizontally or vertically to form a small hole **738** from the perimeter edge **736** to the basin **714** when the mating pieces **712**A and **712**E are placed one on top of the other.

In still another embodiment **810**, the end of the passageway **838** may be attached to a flange **840**. The flange **840** facilitates location of the opening for the refilling of the basin **814** with a medicament by the use of a syringe (not shown). In addition, the use of a flange **840** may prevent or reduce contamination. The flange **840** may be located on the side of the core body **812** or a short distance away and connected by a small tube **842**. The passage way **838** may be formed as a tortuous path as shown in FIG. **7**A.

In complex situations, it may be necessary to place multiple medicaments near the site of the condition or disease. In such cases multiple basins may be formed within the core body **943**, **945**. As shown in FIG. **8**, the core body **912** includes at least a smaller proximal basin **943** and a small distal basin **945** basins with a banded screen, including a different number and different size of holes in the predetermined pattern of holes over each of the proximal **943** and distal **945** smaller basins.

Still other embodiments of the disclosed drug delivery platform appear in FIGS. **9** through **23**, as described below.

In FIG. **9** is shown an embodiment of the drug delivery device **1010** which includes a proximal basin **1043**, a middle basin **1045**, and a distal basin **1047**. The proximal basin **1043** is separated from the middle basin **1045** by use of a first partition **1041**, and the middle basin **1045** is separated from the distal basin **1047** by use of a second partition **1049**. If required, the transport or movement of a medicament between the various smaller basins may be facilitated by passages **1048** formed in the partitions **1041**, **1049**. It is also to be noted that the predetermined pattern of the holes in both the first banded screen **1024** on the upper face **1020** of the core body **1012** and the second banded screen on the lower face **1024** of the core body **1012** is formed for control of the release of medicament. Specifically, a U-shaped pattern of screen holes **1050** is included at the distal end **1015** and an arcuate pattern of screen holes **1052** is included at the proximal end **1013**. This embodiment is particularly useful when it is necessary to place three medicaments, M**1**, M**2**, and M**3** within the body of an animal. Alternatively, the partitions **1041** and **1049** may be solid or impermeable to keep the medicaments M**1**, M**2** and M**3** separate.

FIG. **10** illustrates an embodiment **1110** for the dissipation of two medicaments, M**1** and M**2** within the body. Accordingly, the core body **1112** is divided into a proximal smaller basin **1143** and a distal smaller basin **1147** using a solid or impermeable partition **1141** therebetween. Release of the medication M**2** is controlled by a U-shaped pattern of screen holes **1150** in both the upper banded screen **1124** and in the lower banded screen **1126** over the distal partition **1147**. Over the proximal basin **1143** is located a trapezoidal pattern of screen holes **1154** for controlling the release of the medicament M**1**.

In FIG. **11**, another two-compartmented implantable drug delivery platform **1210** is shown. Note that there is a first pattern of screen holes **1256** within a band **1225** which covers the entire distal basin **1247** and a second pattern of screen holes **1258** within a band **1225** which covers the entire proximal basin **1243** which holds medicaments M**2** and M**1** respectively.

In FIG. **12** is shown an embodiment **1310** with a single basin **1314** for holding a medicament M. The single basin **1314** is formed by the joining together of the two core body pieces, **1312**A and **1312**B. Each of the pieces **1312**A, **1312**B includes a full pattern of screen holes **1360** within a band **1325** to cover the basin **1314** formed between the two portions **1312**A, **1312**B of the core body.

In FIG. **13** is shown yet another embodiment **1410** including a single basin **1414**. In this embodiment **1410**, the core body **1412** includes a lower banded screen **1426** covered by an upper banded screen **1424**. Note that the upper banded screen **1424** fully covers the core body **1412** and is configured with a full predetermined pattern of screen holes **1460** within a band **1425** to cover the entire basin **1414**.

In FIG. **14** is shown yet another single basin embodiment **1510**. In this embodiment, the upper banded screen **1524** has a perimeter **1536** extending downwardly therefrom which fits inside the inside perimeter of the basin **1514** formed in the core body **1512**.

In FIG. **15** is shown yet another embodiment **1610** with a single well **1614**. In this embodiment **1610**, the upper banded screen **1634** includes a downwardly depending flange **1662** which is constructed and arranged to be press fit within the perimeter of the basin **1614** formed within the core body **1612** to extend upwardly to engage a recessed portion in a banded screen **1624**.

In FIG. **16** is shown yet another embodiment **1710** having a single basin **1714**. The single basin **1714** is formed in a core body **1712** which further fits within a core body holder **1712**C. The core body holder **1712**C includes an open portion **1712**C therein which will securely hold the core body **1712**. Covering the basin **1714** within the core body **1712** is an upper banded screen **1724**. The bottom portion of the core body **1712** is formed to be a banded screen.

In FIG. **17** is shown an embodiment **1810** similar to the embodiment **1710** shown in FIG. **16**. However, rather than the core body holder **1812**D having a contiguous perimeter, the core body holder **1812**D is formed to have two prongs forming an open space **1812**D.**1** therebetween. The open space **1812**D.**1** is constructed and arranged to receive the core body **1812**. A groove **1864** captures the two prongs of core body holder **1812**D. Once again, the core body **1812** is covered with a banded screen **1824** and the bottom of the core body **1812** is formed as a banded screen.

In FIG. **18** the disclosed embodiment **1910** includes a core body **1912** which has an upwardly extending flange **1966** which fits into the upper banded screen **1924** so that the upper screen **1924** may be positioned on the core body **1912** over the basin **1914**.

In FIG. **19** is shown an embodiment **2010** including a substantially hollow core body **2012**. Resting on the bottom face **2022** of the substantially hollow core body **2012** is a lower banded screen **2026**, and on the top face **2020** of the core body is an upper banded screen **2026**.

In FIG. **20** is shown an embodiment **2110** including a proximal smaller basin **2143** and a distal smaller basin **2147**. The partition **2141** dividing the proximal smaller basin **2143** from the distal smaller basin **2147** has passages **2148** formed therein for the movement of medicament therethrough. Release of the medicaments M1, M2 is controlled by the predetermined arcuate pattern of holes **2152** formed in both the upper banded screen **2124** and the lower banded screen **2126**. Alternatively, the partition **2141** may run along the long axis of the basin **2114** to form side-by-side smaller basins.

In FIG. **21** is still yet another embodiment **2210** including a proximal smaller basin **2243** and a distal smaller basin **2247**. A partition **2241** divides the proximal basin **2243** from the distal basin **2247** in the core body **2212**. Both the upper banded screen **2224** and the lower banded screen **2226** contain a U-shaped pattern of holes **2250** at the distal end **2215** and a full pattern of holes **2260** at the proximal end **2213**.

In FIG. **22** is shown an oblong thickened embodiment **2310** which includes circular banded screens **2324**, **2326** to be placed on the upper face **2320** and lower face **2322** of the core body **2312**.

Examples

Devices similar to those depicted in FIG. **15** were implanted into eight New Zealand White rabbits. The screen was attached to the core body using a silicone adhesive. The contralateral eye was used as a control. One rabbit was taken out of the study at two days. Three animals were tested at one month, and the remaining four rabbits were tested at three months. Histo-pathological observations were conducted at both one month and three months. At one month, three of the animals exhibited a small number of inflammatory cells in the vitreous. One animal of these three also exhibited minimal inflammation in ora serrata. The final animal had minimally swollen lens fibers. Toxicology observations for this group were unremarkable. Toxicology observations for all of the animals in the three-month sampling were unremarkable.

In an in vitro study, betaxolol HCl, a relatively high water soluble substance, was tableted with 10% microcrystalline cellulose and 0.40% magnesium stearate with a total weight of 22 mg. The betaxolol HCl tablet was inserted into the basin of drug delivery devices similar to the embodiment depicted in FIG. **15**. The devices utilized one 8 micron 1% porosity banded screen on one side of the basin. The ratio of the area of all substantially uniform holes to the area of all surfaces on the drug delivery device was about 0.02%. Loaded drug delivery devices according to the present invention were placed in a 4 mL HPLC vial with phosphate/saline buffer and then stirred using a small stir bar. The vials were periodically sampled and analyzed for drug concentration by HPLC. As shown in FIG. **24** a plot of drug concentrates over time demonstrates the release profiles.

In a second in vitro study, another second drug formulation using a substance with a relatively low water solubility, nepafenac in tablet form, was also studied in a device similar to the embodiment depicted in FIG. **15**. These tablets also contained 10% microcrystalline cellulose and 0.40% magnesium stearate. One tablet was placed in a two-sided 14 micron 25% porosity device. The ratio of the area of the area of all substantially uniform holes to the area of the banded screen was about 4.5%. The ratio of the area of all holes to the area of all surfaces on the drug delivery device was about 0.48%. A second tablet was placed in a two-sided 14 micron 1% device. The ratio of the area of all holes to the are of the banded screen was about 0.18%. The ratio of the area of all holes to the area of all surfaces on the drug delivery device was bout 0.02%. The drug release studies were performed as described above. As shown in FIG. **25**, plot "A" shows the release profile from the two-sided 14 micron 25% porosity device. Plot "B" is the release profile from the two-sided 14 micron 1% porosity device. A third experiment was performed by replacing the phosphate/saline buffer from the two-sided 14 micron 1% porosity device and reinitiating the experiment. This experiment is demonstrated by plot "C."

Operation

Once a medical condition or disease within the body is identified and located, a physician will determine whether or not such condition or medication may be treated with a medicament placed in close proximity to site of the condition or disease. If the decision is made to treat the condition or disease with a medicament placed close to the condition or disease, it then becomes necessary to actually place the medicament near the condition or disease. In other applications, it may be necessary to treat a condition or disease from a short distance. Such short distance treatment may require sustained levels of medicament flow from the drug delivery device.

In the embodiment **10** shown in FIG. **1**, the condition or disease is contained within the eye of a patient. For example, a surgeon may insert an implantable device into the vitreous chamber of a patient by making a small incision in the sclera. The drug delivery platform **10** is then inserted through the incision and held in place by threading a suture through the suture hole **30** in the core body **12** and attaching the other portion of the suture to the eye. The orientation of the platform is such that the implanted platform remains out of the path of light rays from the lens to the retina.

To prevent coating of the implanted devices with cells which can block the movement of medicament from the basin through the empty holes in the banded screen, an anti-proliferative coating may be used on both the screen and core body. Similarly, materials such as silicon may form chips so as to prevent chipping the banded screen, and the core body may be coated with a substance to prevent chipping.

As previously mentioned, while the preferred embodiment is shown for the purpose of inserting medicament to treat a condition or disease within the inner eye, those of ordinary skill in the art will understand that the disclosed implantable drug delivery platform **10** may be used at any location within the body of an animal where a condition or disease is best treated with an implanted medicament.

The present invention, having now been disclosed according to its preferred and alternate embodiments, will now be understood by those of ordinary skill in the art. Those of ordinary skill in the art will understand that numerous other embodiments of the present invention may also be embodied by the foregoing disclosure. Such other embodiments shall be included within the scope and meaning of the appended claims

What is claimed is:

1. An implantable medicament delivery device comprising:

a basin constructed and arranged to contain the medicament, said basin being surrounded by a basin containment portion formed from a non-permeable material;

one or more screens, each screen of the one or more screens including a predetermined pattern of bi-directional flow empty holes for controlling the free flow of dissolved medicament therethrough, each pattern of holes of each screen being encircled by a band constructed and arranged to cover the top or bottom of said basin when said band is affixed to said basin containment portion, each screen of the one or more screens having a thickness from about 0.05 mm to about 0.5 mm and said bi-directional flow empty holes having a size from about 0.2 microns to about 100 microns;

wherein the bi-directional flow empty holes assure that a required amount of medicament is delivered at a needed flow rate therethrough and wherein said flow rate is based upon one or more factors selected from the group including solubility of the medicament, medicament dissolution rate and medicament concentration and wherein the bi-directional flow empty holes are the exclusive mechanism for controlling the free flow of dissolved medicament and wherein the basin is arranged to contain the medicament without containing any plunger or alternative device for aiding flow of the dissolved medicament.

2. The implantable medicament delivery device as defined in claim **1** wherein the one or more screens include at least two screens.

3. The implantable medicament delivery device as defined in claim **1** wherein said basin passes through said basin containment portion.

4. The implantable medicament delivery device as defined in claim **1** wherein said basin containment portion is substantially planar.

5. The implantable medicament delivery device as defined in claim **1** wherein said basin includes a plurality of sections separated by an impermeable barrier.

6. The implantable medicament delivery device as defined in claim **1** wherein said one or more screens are made from silicon.

7. The implantable medicament delivery device as defined in claim **2** wherein said basin is made from silicon.

8. The implantable medicament delivery device as defined in claim **2** wherein said at least two screens are made from silicon.

9. A device for delivering medicament within the body of an animal in close proximity to a condition treatable by said medicament, said device comprising:

a basin containment portion having a first face, a second face, a perimeter, and a medicament basin between said first face and said second face of said basin containment portion being formed from a non-permeable material;

one or more screens, each screen of the one or more screens including a predetermined pattern of bi-directional flow empty holes for controlling the release of dissolved medicament therethrough, each pattern of holes of each screen being encircled by a band, said band being affixed to said first face or said second face of said basin containment portion near the intersection of said basin respectively with said first face or said second face of said basin containment portion;

each screen of the one or more screen having a thickness from about 0.05 mm to about 0.5 mm and said bi-directional flow empty holes having a size from about 0.2 microns to about 100 microns;

wherein the bi-directional flow empty holes assure that a required amount of medicament is delivered at a needed flow rate therethrough and wherein said flow rate is based upon one or more factors selected from the group including solubility of the medicament, medicament dissolution rate and medicament concentration and wherein the bi-directional flow empty holes are the exclusive mechanism for controlling the free flow of dissolved medicament and wherein the basin is arranged to contain the medicament without containing any plunger or alternative device for aiding flow of the dissolved medicament.

10. The device as defined in claim **9** wherein the one or more screens include at least two screens.

11. The device as defined in claim **10** wherein said basin in said basin containment portion includes a plurality of smaller basins separated one from another by an impermeable wall.

12. The device is defined in claim **9** wherein said one or more screens are made from silicon.

13. The device is defined in claim **10** wherein said at least two screens are made from silicon.

* * * * *

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 7,621,907 B2
APPLICATION NO. : 10/385791
DATED : November 24, 2009
INVENTOR(S) : Theron Robert Rodstrom

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

On the Title Page:

The first or sole Notice should read --

Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 504 days.

Signed and Sealed this

Twenty-sixth Day of October, 2010

David J. Kappos

David J. Kappos
Director of the United States Patent and Trademark Office